

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number
WO 2004/042406 A1

- (51) International Patent Classification⁷: **G01N 33/68, 33/574**
- (21) International Application Number:
PCT/EP2003/012295
- (22) International Filing Date:
4 November 2003 (04.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
0225799.6 5 November 2002 (05.11.2002) GB
60/495,309 14 August 2003 (14.08.2003) US
- (71) Applicant (for all designated States except US): **NOVARTIS FORSCHUNGSSTIFTUNG, ZWEIGNIEDERLASSUNG FRIEDRICH MIESCHER INSTITUTE FOR BIOMEDICAL RESEARCH [CH/CH];** Maulbeerstrasse 66, CH-4058 Basel (CH).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **BADACHE, Ali [FR/FR];** 27, rue du Stade, 68170 Rixheim (FR). **HYNES, Nancy [US/CH];** Lerchenstrasse 2, CH-4059 Basel (CH). **SCHICK, Nicole [DE/DE];** Denkmalstrasse 2, 67251 Freinsheim (DE).
- (74) Common Representative: **NOVARTIS FORSCHUNGSSTIFTUNG, ZWEIGNIEDERLASSUNG FRIEDRICH MIESCHER INSTITUTE FOR BIOMEDICAL RESEARCH;** Maulbeerstrasse 66, CH-4058 Basel (CH).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TEL/ETV6-MEDIATED INHIBITION OF CELL PROLIFERATION

(57) Abstract: A method of modulating Stat3-dependent and cytokine-sensitive cell proliferation is provided, as well as screening methods for agents affecting Stat3-dependent and cytokine-sensitive cell proliferation. The method is exemplified by modulating TEL/Etv6.

WO 2004/042406 A1

INTERNATIONAL SEARCH REPORT

Inte nal Application No

PO 03/12295

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHAKRABARTI SUBHRA R ET AL: "The leukemia-associated gene TEL encodes a transcription repressor which associates with SMRT and mSin3A" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 264, no. 3, 2 November 1999 (1999-11-02), pages 871-877, XP002269663 ISSN: 0006-291X cited in the application Material and Methods section	17
A	---	1-16, 20-29
	--- -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

18 February 2004

Date of mailing of the international search report

03/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Jacques, P

INTERNATIONAL SEARCH REPORT

Inte al Application No
PC 03/12295

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VAN ROMPAEY L ET AL: "Tel induces a G1 arrest and suppresses ras-induced transformation" ONCOGENE, vol. 19, no. 46, 2 November 2000 (2000-11-02), pages 5244-5250, XP002269664 ISSN: 0950-9232 cited in the application Materials and Methods section	17
A	----	1-16, 20-29
X	WO 01 36646 A (EVANS MARTIN JOHN ;WIANNY FLORENCE (GB); CANCER RES CAMPAIGN TECHN) 25 May 2001 (2001-05-25) page 4, line 19 - line 24 page 9, line 27 -page 11, line 5	20-23, 25-29
Y	page 11, line 26 -page 12, line 2	24
X	WO 99 32619 A (CARNEGIE INST OF WASHINGTON ;MONTGOMERY MARY K (US); FIRE ANDREW () 1 July 1999 (1999-07-01) page 9, line 14 - line 28	20-23, 25-29
Y	page 15, line 17 -page 16, line 27	24
Y	OCKERT D ET AL: "Advances in cancer immunotherapy" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 20, no. 2, February 1999 (1999-02), pages 63-65, XP004157277 ISSN: 0167-5699 the whole document	24
A	BROMBERG JACQUELINE: "Stat proteins and oncogenesis" JOURNAL OF CLINICAL INVESTIGATION, vol. 109, no. 9, May 2002 (2002-05), pages 1139-1142, XP002269665 ISSN: 0021-9738 the whole document	1-17, 20-29
A	PARMIANI GIORGIO ET AL: "Cytokines in cancer therapy" IMMUNOLOGY LETTERS, vol. 74, no. 1, 15 September 2000 (2000-09-15), pages 41-44, XP002269666 ISSN: 0165-2478 the whole document	1-17, 20-29
	----- -/--	

INTERNATIONAL SEARCH REPORT

Int. Application No

PC 03/12295

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LACRONIQUE VIRGINIE ET AL: "Transforming properties of chimeric TEL-JAK proteins in Ba/F3 cells" BLOOD, vol. 95, no. 6, 15 March 2000 (2000-03-15), pages 2076-2083, XP002269667 ISSN: 0006-4971 the whole document	1-17, 20-29
A	MAVROTHALASSITIS GEORGE ET AL: "Proteins of the ETS family with transcriptional repressor activity" ONCOGENE, vol. 19, no. 55, 18 December 2000 (2000-12-18), pages 6524-6532, XP002269668 ISSN: 0950-9232 the whole document	1-17, 20-29
A	BOWMAN T ET AL: "STATS IN ONCOGENESIS" ONCOGENE, BASINGSTOKE, HANTS, GB, vol. 19, no. 21, 15 May 2000 (2000-05-15), pages 2474-2488, XP009003623 ISSN: 0950-9232 the whole document	1-17, 20-29

FURTHER INFORMATION CONTINUED FROM PCT/ISA 210

Continuation of Box I.2

Claims Nos.: 18-21, 25,26, 29-30

Present claims 18-21, 25-26 and 29-30 relate to a method using a compound defined by reference to a desirable characteristic or property, namely being an activator or inhibitor of TEL activity, thus being identifiable by the method of claims 1 and 6.

However, no technical features of the compound are given in the claims. The skilled person is therefore unable to understand which compounds should be used in the claimed methods. The claims lack thus clarity as to render a meaningful search over the whole of the claimed scope impossible. The description provides technical features for only a very limited number of such compounds, namely RNAi and antibodies.

Consequently, the search has been carried out for those parts of the claims which appear to be clear. Therefore, Claims 20-21, 25-26 and 29 have been searched when relating to inhibitors as defined in the description on page 19, second paragraph and in claims 22 and 24, namely RNAi and inhibitory antibodies.

As no exemple or reference to an activator of TEL is mentioned in the application, claims 18-19 and 30 have not been searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/12295

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 18 to 28 encompass in vivo methods, thus falling under the concept of methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 18-21, 25, 26, 29-30
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP03/12295

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0136646 A	25-05-2001	AU 1406501 A	30-05-2001
		CA 2391622 A1	25-05-2001
		DE 1230375 T1	09-01-2003
		EP 1230375 A1	14-08-2002
		WO 0136646 A1	25-05-2001
		JP 2003514533 T	22-04-2003
		NO 20022359 A	18-07-2002
		US 2003027783 A1	06-02-2003
WO 9932619 A	01-07-1999	ZA 200203816 A	02-01-2003
		US 6506559 B1	14-01-2003
		AU 743798 B2	07-02-2002
		AU 1938099 A	12-07-1999
		CA 2311999 A1	01-07-1999
		EP 1042462 A1	11-10-2000
		JP 2002516062 T	04-06-2002
		WO 9932619 A1	01-07-1999
		US 2003056235 A1	20-03-2003
		US 2003051263 A1	13-03-2003
		US 2003055020 A1	20-03-2003